

REMARKS

Claims 2-5 and 13-15 are pending in the application. The amendments to the claims have been made to further clarify the present invention and conform to U.S. practice. No new matter has been inserted into the application. No new issue is raised requiring further search or consideration since the amendments to the claims serve to place the application in better condition for allowance. Accordingly, entry of the amendments to the application is respectfully requested.

Interview Summary

Applicants' undersigned representative acknowledges receipt of Examiner's Interview Summary mailed April 18, 2003.

Claim Objections

Claim 14 has been objected to because of an informality. Appropriate correction has been made as required by the Examiner. Therefore, this objection has been overcome.

Rejections Under 35 USC § 112, first paragraph – new matter

Claims 2-5 and 13-15 have been rejected under 35 USC § 112, first paragraph, as containing subject matter which was not described in the specification and introducing new matter. The Examiner has rejected claim 13 because the limitation of treating osteoarthritis with chondrocytes transfected with TGF- β or BMP is new matter. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

Applicants submit that claim 13 is directed to a method of regenerating hyaline cartilage, not to a method of treating osteoarthritis. Therefore it is believed that this rejection is misplaced.

The Examiner has also objected to the phrase “transfected/transduced” in claims 4, 5 and 13 as being new matter. The amended claims recite “transfected”. Accordingly, this objection has been overcome.

Rejections Under 35 USC § 112, first paragraph – enablement

Claims 2-5 and 13-15 have been rejected under 35 USC § 112, first paragraph because “the specification, while being enabling for transfecting chondrocytes with DNA encoding TGF- β 1 operably linked to a promoter, transplanting the transfected chondrocytes into a joint space of a mammal such that expression of TGF- β 1 occurs resulting in generating hyaline cartilage, does not reasonably provide enablement for using chondrocytes encoding BMP to regenerate hyaline cartilage as broadly claimed.” Page 3, Office Action of January 29, 2003. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested. However, the amended claims are directed to chondrocyte comprising DNA encoding TGF- β 1 operably linked to a promoter, which the Examiner has determined is enabled by the specification. Thus, it is believed that the rejection has been overcome.

Rejections Under 35 USC § 112, second paragraph – indefiniteness

Claims 2-5 and 13-15 have been rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter. The Examiner has objected to claims 4, 5 and 13 because the phrase “transfected/transduced” is unclear. The amended claims recite “transfected”. Accordingly, this objection has been overcome.

The Examiner has objected to claims 4, 5 and 13 because the phrase “chondrocyte cells” is indefinite. The amended claims recite “chondrocytes”. Accordingly, this objection has been overcome.

Rejections Under 35 USC § 103

Claims 2-5 and 13-15 have been rejected under 35 USC § 103 (a) as being obvious over Naughton (US Patent 5,842, 477, Dec. 1, 1998) in view of Ikeda (Sept. 1998, J. Rheumatol., Vol. 25, Pg 1666-1673) and van Beuningen (Sept. 1998, Osteoarthritis and Cartilage, Vol. 6, pg 306-317). Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

The Present Invention

The present invention is directed to a method of generating hyaline cartilage, comprising:

- a) generating a recombinant viral or plasmid vector comprising a DNA sequence encoding transforming growth factor β 1 (TGF- β 1) operatively linked to a promoter;
- b) transfecting *in vitro* a population of chondrocytes with said recombinant vector, resulting in a population of transfected connective tissue cells; and
- c) injecting a composition consisting of the transfected population of chondrocytes and a pharmaceutically acceptable carrier into a joint space of a mammal such that expression of the DNA sequence encoding TGF β 1 within the joint space occurs resulting in the generation of hyaline cartilage in the joint space.

Naughton '477

Naughton '477 discloses placing an artificial framework such as a scaffold together with periosteal/perichondral tissue and stromal cells near the cartilage defect region such that stromal cells are partly trapped in the scaffold. However, Naughton '477 fails to disclose or suggest injecting a chondrocyte composition into the joint without the use of an artificial framework.

Ikeda

Ikeda discloses intra-articularly injecting TGF β 1 containing adenovirus in an *in vivo* gene therapy methodology. However, Ikeda fails to disclose or suggest a cell-mediated gene delivery system as in the presently claimed invention.

van Beuningen

van Beuningen discloses increased proteoglycan synthesis by injecting the protein form of TGF β 1. However, van Beuningen fails to disclose or suggest a cell-mediated gene delivery system.

Distinctions of the present invention over the cited references

Naughton '477 suggests administering a composition comprising chondrocytes in the presence of scaffolding and a pharmaceutically acceptable carrier into a joint space of a mammal such that cartilage is generated.

The present invention is directed to generating hyaline cartilage by injecting a composition that consists of transfected chondrocytes and a pharmaceutically acceptable solution, and excludes compositions of transfected chondrocytes, scaffolding and a pharmaceutically acceptable solution. Accordingly, the Naughton '477 reference fails to be relevant to the presently claimed invention. Ikeda and Van Beuningen fail to remedy the deficiencies in the Naughton '477 reference in their failure to disclose or suggest using the inventive composition to generate hyaline cartilage. Accordingly, the presently claimed invention is not obvious over the cited references.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to JHK Law's Deposit Account No. 502486 during the pendency of prosecution of this application. Should such additional fees be associated with


an extension of time, applicant respectfully requests that this paper be considered a petition therefor. A duplicate of this paper is enclosed for the Deposit Account, should it be needed.

Respectfully submitted,

JHK Law

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By: _____


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